

DISEASES OF THE LYMPHOID TISSUE OF THE
CONJUNCTIVA.*

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A PAPER dealing with diseases of the lymphoid tissue of the conjunctiva might readily lead to a discussion of all the inflammatory affections of that membrane, for in all of them the fibro-adenoid layer becomes implicated. It is, however, mainly diseases which are characterised by marked over-development of lymphoid tissue which I propose, in opening this discussion, to describe, and especially the most serious of these—trachoma.

Trachoma is a disease of such exceedingly long duration that few observers have the opportunity of watching cases from the commencement to the finish. In this respect I have had exceptional advantages. The Metropolitan Asylums Board has established Ophthalmia Schools for the isolation of children who, while under the charge of the Poor Law Authorities in London, are found to be suffering from any contagious eye disease. The number of children admitted to these schools in the past five years, during which time I have held the appointment of Ophthalmic Surgeon to them, has been 2441, of which 700 were suffer-

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ing from trachoma. In many of these cases the disease has been in an exceedingly early stage. The children have been sent for admission, not because they made any complaint of their eyes, but because the medical officers of their parish schools noticed some abnormal discharge from them. The children when admitted to the Ophthalmia Schools are kept there, unless their parents insist on taking them out, until they can be certified as cured. It will be seen, then, that these schools afford excellent advantages for the study of the natural history and treatment of trachoma. It is the outcome of the experience which I have gained at them that I now propose to lay before you.

That trachoma is a contagious disease has been proved by inoculation experiments. I have had, however, some very definite confirmatory evidence. When first one of these ophthalmia schools was started, a "house mother" and an assistant nurse employed there contracted trachoma. In one case there was the history of some water having splashed into the woman's eye while she was engaged in washing a child who had trachoma, and it was from that time that the onset of the affection dated.

The way in which the disease started in these two cases is of interest, because they were seen from the very commencement. In both, the symptoms at first resembled those of an acute mucopurulent ophthalmia. There was swelling and redness of both ocular and palpebral conjunctiva, some papillary enlargement of the latter, and mucopurulent discharge. The symptoms, however, did not yield to treatment in the satisfactory way which is usual in that affection, and when the congestion of the palpebral conjunctiva had somewhat subsided the typical lymphoid follicles in the tarsal conjunctiva and the retrotarsal folds became apparent. In one case the affection remained confined to one eye, in the other both eyes ultimately became involved. Both cases were cured after about eighteen months' treatment.

The Ophthalmia Schools are arranged in what is known as the cottage system. They are situated, one at Swanley, in

Kent, and the other at Brentwood, in Essex, and have large and beautiful grounds. Some of the children when their eyes are cured are very loth to depart from these pleasant surroundings to return to their parish barraek schools in London. Various tricks are played by them to keep up discharge from their eyes, or to make them injected, so that they may not be sent away. One child, whose name peculiarly enough was Sly, was admitted with marginal blepharitis and slight conjunctivitis; this was cured and all treatment was stopped preparatory to her leaving the school. She was then caught by the nurse taking discharge from another child's eye who was suffering with trachoma and deliberately putting it into her own. The symptoms of acute mucopurulent ophthalmia rapidly set in, and two months later typical trachoma follicles on the tarsal conjunctiva were recognised. After a year's treatment the trachoma was cured. The contagious character of trachoma being definitely established, there can be little doubt that the contagious element is some micro-organism.

During the last two years, Prowazek and Greeff, working independently, have discovered in the cells from the trachomatous conjunctiva, by the use of Giemsa staining methods, minute slightly ovoid bodies considerably smaller than the smallest of the known cocci. They are found massed together in the cells near the nucleus in the form of a cap, but separated from it by a clear space. The enclosure containing the granules enlarges rapidly, causing the cell to swell and ultimately burst, the granules then being discharged. So far these parasites, if such they are, have not been cultivated or made to reproduce the disease, the evidence in favour of their being the specific organism of trachoma resting on the frequency with which they have been found in cases of that disease, and in the failure to find them in other affections.

Whatever may be the contagious element of trachoma, we may feel sure that it is one which is not spread through the air; that it is, like many of the other organisms which

give rise to contagious ophthalmia, easily killed by drying, and not spore-producing.

Individuals may live surrounded by those suffering from the disease and by the observance of a few simple precautions never become affected. At the Ophthalmia Schools there are employed a large staff of nurses, teachers, and attendants, but the two cases referred to are the only ones of trachoma which have arisen amongst them. If the contagion could be carried in the form of dust in the air, more of the attendants, or I myself who look closely into all the children's eyes every ten days, should surely have become affected.

In countries such as Egypt, where the majority of the native population suffer from the disease or its sequelæ, the Europeans who visit the country and observe precautions as regards cleanliness, which are quite foreign to the natives, rarely contract it. All the evidence, I think, tends to show that it is the transference of moist discharge from one person's eye to another which disseminates the disease.

In some diseases of the conjunctiva, due to microbial infection, *e.g.*, gonorrhœal ophthalmia and diplobacillary ophthalmia, the organism is found chiefly in the epithelium. In others, *e.g.*, tuberculosis, the organism is located, not in the epithelium but in the sub-epithelial tissue. A comparison of the histological characters of a tubercular nodule of the conjunctiva with those of a trachoma follicle would suggest that the position in which the trachoma organism is usually situated is, like that of the tubercle bacillus, the fibro-adenoid layer.

A tubercle nodule and a trachoma follicle both consist of an aggregation of cells, the most peripheral of which are small lymphocytes and the more central of the epithelioid type. In the centre of a tubercle nodule is the characteristic giant cell, with peripheral arranged nuclei and degenerate cytoplasm, in which the tubercle bacilli are found. In the centre of a trachoma follicle there is no giant cell, but the epithelioid cells are there most degenerate. It would seem,

therefore, to be the position where the toxine is most intense and where the organism generating that toxine would most likely be situated.

Mayou* has further pointed out that in a trachoma follicle plasma cells are absent, though occasionally found in its outer zone. As there is good evidence to show that plasma cells are not very resistant to toxines this arrangement of them is further evidence that the intensity of the toxine is greatest in the centre of the follicle.

Prowazek insists that the ovoid bodies which he has found in cases of trachoma are met with only in the epithelial not in the lymphoid cells. Greeff states that after a case has been treated with sulphate of copper these bodies disappear from the superficial cells and the secretion long before the case is cured. He suggests that they pass into the deeper parts where they can still excite changes.

Some micro-organisms we know, like the gonococcus, can attack the intact epithelium of a mucous surface. Whether or not the organism of trachoma is able to do this cannot yet be determined. The not uncommon accompaniment of trachoma in its early stages with an acute conjunctival inflammation, which is found to be due to Koch-Weeks bacillus or the gonococcus, suggests that breaks in the continuity of the epithelium, or softening of it, may facilitate the passage of the trachoma organism into the adenoid layer; a mixed infection of the two diseases having been implanted at the same time.

Wherever the trachoma organism is located the changes which it or its toxines excite are most marked in the adenoid layer of the tarsal conjunctiva and the retrotarsal folds, *i.e.* in those parts of the conjunctiva over which the epithelium is thinnest.

Most observers speak of the upper retrotarsal fold as the part which is generally first affected. Having seen, as already stated, many very early cases of the disease, I am inclined to consider the appearance of grey, scattered,

* Changes produced by Inflammation in the Conjunctiva, 1905, p. 116.

avascular spots, rather smaller than a pin's head, in the tarsal conjunctival of the upper lid, as quite as early a symptom as the presence of follicular enlargements in the upper retrotarsal fold.

These grey spots have been termed "elementary or primary granulations" (v. Graefe, Jacobson). Their appearance is quite characteristic and of considerable diagnostic importance. Their presence, when there is much mucopurulent ophthalmia in association with the trachoma, and consequently considerable congestion and papillary enlargement, is often obscured from view, and it is not until these other symptoms have subsided that they become visible.

There are some microbial diseases of the conjunctiva, like gonococcal infection and Koch-Weeks bacillus infection, in which the chief effect of the toxin is the outpouring of a large number of polymorphonuclear leucocytes which infiltrate the tissue and form the predominant cellular element in the discharge. These leucocytes have marked phagocytic powers, and the organisms may be found in the cells in various stages of digestion.

In another microbial disease, viz., diplobacillary conjunctivitis, Stock, Mayou,* and Brown Pusey† have shown that there is little or no increase in either polynuclear or mononuclear leucocytes, but a large increased growth of epithelium, and the formation immediately beneath the epithelium of a number of plasma cells. The discharge is not purulent but consists of mucin, from increased activity of the epithelium, degenerate epithelial cells and the bacilli.

The trachoma organism would also appear to be a non-pyogenic one, the reaction which is excited by its toxine being an immense new formation of lymphoid tissue, a large increase of plasma cells, and in the latter stages a formation of fibroblasts. Though in many cases of trachoma some polynuclear leucocytes are found in the discharge, they do not appear to be a consistent element, and when present can

* Changes produced by Inflammation in the Conjunctiva, 1905, p. 102.

† Archives of Ophth., vol. xxxviii, No. 1, 1909, p. 8.

usually be attributed to infection with other organisms or the presence of other chemiotactic substance. Mayou has pointed out that a characteristic of smear preparations obtained from trachomatous conjunctiva by gentle friction is the presence of an enormous number of plasma cells.

Trachoma *per se* is essentially a chronic disease, the acute symptoms which sometimes usher in an attack, or which arise from time to time in the course of it, can always be accounted for by mixed infection. In the trachoma cases admitted to the Ophthalmia Schools I have frequently found organisms in the discharge, such as Koch-Weeks bacillus and staphylococci, and when by appropriate treatment these have been eliminated, the trachoma has remained as a chronic disease. In these Schools, where the children's eyes are regularly bathed and attended to several times a day by skilled attendants, acute exacerbations of symptoms are very uncommon.

Koch, while in Egypt in 1883, found in the conjunctival discharge in trachoma cases two different kinds of micro-organisms, the gonococcus and what is now known as the Koch-Weeks bacillus. As neither of these is the specific organism of trachoma, the cases must be regarded as having had a mixed infection.

The descriptions which are given of the outbreak of ophthalmia in this country in 1801 and 1802 as the result of the return of Sir Ralph Abercromby's troops from Egypt, is that of an acute purulent ophthalmia with rapid destructive ulceration of the cornea. Some of the cases later on, however, presented the characteristic cicatricial contraction and pannus of trachoma. I think that there can be little doubt that these cases were of a mixed character, of gonorrhoeal ophthalmia plus trachoma.

I think it is incorrect and misleading to speak, as so many of the text-books do, of two types of trachoma, a papillary type and a follicular type. The essential element of trachoma is the follicle; it is the characteristic form of reaction on the part of the tissue to the irritation of the

trachoma organism. Papillary formation over the tarsal conjunctiva, on the other hand, is present in many acute and chronic inflammatory affections. It may, it is true, exist with the follicles in trachoma and sometimes be so extensive as to obscure them, but without the presence of lymphoid follicles we have no right to diagnose a case as one of trachoma.

A characteristic of the trachoma follicles is their tendency to become confluent and produce bodies resembling in shape the grains of boiled sago. This running together of the follicles is most met with in the loosely attached tissue of the retrotarsal folds, but may occur in severe and more advanced cases in the more firmly attached tarsal conjunctiva. As the follicles increase in size the epithelium overlying them becomes thinned and the central part disintegrates until ultimately they rupture, gelatinous contents escaping. On everting the lids in an advanced case of trachoma, many follicles may often be seen just on the point of rupturing and with a very little pressure their contents can be extruded.

Microscopical examination of a follicle which has been ruptured by expression shows (as pointed out by Mayou) invasion of its walls and cavity by polynuclear leucocytes, due, he suggests, to the presence of septic organisms from the conjunctival sac, or possibly I would suggest to chemio-tactic action set up by products eliminated from the damaged epithelial cells.

It has been long recognised that chronic cases of trachoma may be considerably benefited by an acute inflammatory attack. Microscopically it has been found that the trachoma follicles may become invaded from the periphery by polynuclear leucocytes. Such cells do not form part of what may be considered the normal constituents of a trachoma follicle. When, however, an exudation of these highly phagocytic cells is brought about by pyogenic organisms, or the application to the conjunctiva of some irritant such as jequirity, or sulphate of copper, they will invade the follicles and effect their absorption.

Besides the follicular formation in trachoma there is a considerable formation of plasma cells immediately beneath the epithelium between and beneath the follicles; also in the later stages a formation of fibroblasts. I do not propose to enter into the vexed question as to the origin of plasma cells: every possible origin has found its advocate who has supported his view for more or less plausible reasons. Their ultimate fate is also to some extent a moot point, there being a difference of opinion as to whether or not they are capable of developing into fibrous tissue. In the later stages of some cases plasma cells may undoubtedly break down and produce a hyaline material which gives rise to the condition known clinically as "Stellwag's brawny œdema." In its portions, sometimes large areas, of the palpebral conjunctiva have a smooth surface and waxy gelatinous appearance. This condition is similar to, though more extensive than, the milky, opalescent, appearance of the surface of the conjunctiva met with in spring catarrh, which is produced, not as was at one time thought by a thickening of epithelium, but by a hyaline degeneration of plasma cells immediately beneath the epithelium.

The fibrous tissue which forms in trachoma is probably mainly developed from fibroblasts derived from connective tissue cells. It makes its appearance either as strands and irregular networks, or over a large area, which loses its transparency and becomes a dull yellowish white colour. The formation of fibrous tissue and of areas of hyaline degeneration are often associated in the later stages of the disease. The fibrous tissue as it forms replaces the adenoid layer; it destroys the trachoma follicles, partly by forcing them to the surface, where they rupture, and partly by compressing them, and in its contraction causing them to shrink. Some small superficial scar areas are no doubt formed at the seat of the ruptured follicles, but the most extensive growth of fibrous tissue begins in the deeper layers of the membrane and extends forwards to the epithelium.

It is possible for very extensive replacement of the

adenoid layer by fibrous tissue to take place without much distortion of the lid being produced. It is the formation of fibrous tissue in the form of a longitudinal band along the line of the sulcus sub tarsalis (Arlt's Scar streak) which most frequently gives rise to entropion and boat-shaped lid.

It is worthy of note that, in cases where there has been extensive formation of fibrous tissue, the condition of the conjunctiva comes to resemble very closely that of the skin. The palpebral conjunctiva differs from skin in the following three particulars:—

(i) The thinness of the epithelium. Over the tarsus the epithelium of the conjunctiva has only two layers of cells; there is no prickle layer and no keratinised layer.

(ii) The absence of papillæ.

(iii) The presence of the adenoid layer immediately beneath the epithelium instead of the dense fibrous tissue of the corium.

The reason for the reduction of the epithelium of the tarsal conjunctiva to such extreme thinness is, I would suggest, to allow the blood in the rich vascular plexus of the adenoid layer to impart warmth to the avascular cornea when the lids are closed. The absence of papillæ allows the smooth working of the two surfaces of the conjunctiva in contact with one another with a minimum amount of friction, which is further facilitated by the mucus secreted from the rupture of the goblet cells.

The thinness of the epithelium of the conjunctiva exposes it to greater risk of microbial infection than the skin. The lymphoid tissue, or the potentiality for the formation of lymphoid tissue, immediately beneath the epithelium, limits the risk of general systemic involvement from any such infection.

In severe and long standing cases of trachoma, fibrous tissue is formed immediately beneath the epithelium of the palpebral conjunctiva, similar to that of the corium of the skin, which like it is raised into papillæ. Instead of being

composed of only two layers of cells the epithelium is thickened into several layers, the surface ones being flattened and squamous; it also sends down numerous finger-like processes between the papillæ. In some cases these processes are converted into gland-like structures, the orifices of which may become occluded, small retention cysts being formed. These little retention cysts are seen clinically as small yellow-coloured patches about the size of a pin's head. If from the contraction of the new-formed fibrous tissue the ducts of the lacrymal and other conjunctival glands become obliterated, so that the membrane is no longer kept moist, then its resemblance to skin becomes still more marked, keratinised layers of epithelial cells being formed on the surface, and the condition termed xerosis being established.

It is frequently asserted that all cases of trachoma result in the formation of fibrous tissue, or cicatrisation as it is termed. The formation of fibrous tissue is, however, one of the later phenomena of the disease; and it would seem reasonable to suppose that if cases are treated sufficiently early they might sometimes be cured without its occurrence. When follicles come to the surface and rupture, whether spontaneously or as the result of mechanical expression, a small scar is probably formed at the seat of rupture. Scars thus formed may, however, be so infinitesimally small as to be quite invisible clinically. "The elementary or primary granulations" met with in the tarsal conjunctiva may, I am quite sure, as the result of treatment, become absorbed and disappear without leaving any trace of previous existence behind. I have seen several cases treated at the Ophthalmia Schools for characteristic trachoma follicles in the tarsal conjunctiva and retrotarsal folds, which, on leaving, have shown no sign of fibrous tissue formation sufficient to have revealed the fact that they had suffered from the disease.

The use of the term cicatrisation for the new formation of fibrous tissue which develops deeply and replaces the adenoid layer is not, I think, a very appropriate one; it would, I suggest, be better termed a sclerosis.

There has been much discussion as to whether the vascular affection of cornea which is met with in trachoma, termed "pannus," is the result of irritation from a roughened eyelid or a real infection of the cornea with trachoma. I would suggest that it is the outcome of both.

Raehlmann* has found pathologically in the anterior layers of a cornea affected with pannus, lymphoid follicles having the same characteristics as those met with in the lids in trachoma. Mayou has also found them in the conjunctiva removed from the limbus by the operation of peritomy for the relief of pannus.

The conjunctiva covering the sclerotic rarely becomes affected with trachoma except at the corneal margin. The question then arises, why should the bulbar conjunctiva be freer from infection than the tarsal conjunctiva, the retrotarsal folds, and cornea? It might be suggested that the tarsal conjunctiva and retrotarsal folds become affected because they contain lymphoid tissue, and that the bulbar conjunctiva escapes because it does not. If this is so, why, then, should not the cornea also escape, which is most certainly devoid of any lymphoid tissue? If, on the other hand, it is argued that it is the thin covering of epithelium on the tarsal conjunctiva and in the retrotarsal folds which predisposes them to infection, why should the limbus and the cornea, which has thicker laminated epithelium than the bulbar conjunctiva, be more frequently affected than the bulbar conjunctiva? I think an explanation may be found in the damage which must be inflicted to the pliable corneal epithelium by the friction of a roughened lid or in-turning eyelashes over it. In places some of its cells will become brushed away and irregularities will be formed. Into such abrasions the infective trachomatous material becomes subsequently rubbed by the friction of the lids, and so breaks through the protection which the surface epithelium always affords the cornea from external influences.

The formation of lymphoid tissue in a structure like the

* *Archiv für Ophthl.*, Bd. xxiii, 1887, Ab. 3.

cornea, devoid of any normal lymphoid tissue, serves to show that a trachoma follicle is not a mere hypertrophy of pre-existing lymphoid tissue; but that it is a new production for the purpose of defence against the attacking organism.

A study of the natural history of trachoma, as above described, serves to show that the lymphoid follicles which form in connection with it are eliminated in three different ways:

(a) By rupture of the follicles on the surface and discharge of their contents.

(b) By intercurrent inflammation causing follicles to become invaded with polynuclear leucocytes and absorbed.

(c) By the replacement of the adenoid layer by fibrous tissue, which, cutting off the blood supply to the follicles, causes them to atrophy.

Of the immense number of different treatments which have been employed for trachoma, those which have proved most efficacious can, I think, be shown to aid in getting rid of the lymphoid tissue in one of the three above-mentioned ways.

In the operation of expression a large number of follicles are ruptured, and their contents evacuated. If, immediately after expression, the surface of the ruptured follicles is painted with a 1-in-100 solution of perchloride of mercury, an exudate into them of polynuclear phagocytic leucocytes is excited which promotes absorption of the remains of the follicles.

In the operation of expression I prefer to use the flat Grady's forceps rather than Knapp's roller forceps. With the latter I find, unless exactly the right amount of pressure is made, there is a tendency to tear the tissue. My endeavour always is to squeeze, and not to tear. I find a pair of forceps similar to Grady's, which Mr. Tyrrell has had made with a more acute bend, exceedingly useful in catching hold of the upper retrotarsal fold at the inner angle, a position in which a number of follicles are frequently met with.

In performing the operation I employ two pairs of expression forceps, holding the upper lid everted with one pair, and with the other grasping the retrotarsal fold and squeezing the follicles out of it. In the tarsal conjunctiva it is frequently impossible to get rid of the follicles by expression, owing to its firm attachment to the tissue beneath. The so-called "elementary or primary granulations" cannot be squeezed out of the tarsal conjunctiva. To get rid of all the lymphoid follicles from the retrotarsal fold it is often found necessary to repeat the procedure of expression at several different sittings. Even when all follicles seem to have been completely removed from the retrotarsal fold, if the disease is not cured in other parts of the conjunctiva, fresh ones make their appearance which in their turn have to be expressed.

The operation devised by Galezowski of excision of the retrotarsal folds is a very effectual way of getting rid of the follicles and shortening the duration of the disease. I have performed it several times, in cases where there has been much redundance of tissue behind the tarsus. In some cases I have removed all four retrotarsal folds with satisfactory results.

Kuhnt's operation of removal of the tarsus and conjunctiva which covers it I have not performed, not having met at the Ophthalmia Schools with cases which I thought sufficiently severe to justify the employment of so radical a procedure.

Time-honoured sulphate of copper still, I think, maintains the foremost place as the best application in trachoma to stimulate the absorption of follicles which cannot be removed by expression. The reason why a copper salt proves specially useful for this purpose is, I think, to be found in the experiments of Leber. He introduced into the anterior chambers of the eyes of rabbits sterilised substances of different chemical characters, and found different kinds of reaction followed. Thus pieces of gold and glass excited no inflammation, slowly becoming encapsuled by a delicate

connective tissue. Pieces of copper or drops of quicksilver, introduced in precisely similar manner, gave rise to a localised suppuration; whilst croton oil and cantharides caused no pus formation, but a fibrinous exudate with necrosis of tissue.

Copper or its salts then applied to the conjunctiva in a similar way probably set up a mild aseptic purulent inflammation, *i.e.* an exudate of polynuclear leucocytes which will invade the trachoma follicles and tend to bring about their absorption.

In several cases I have endeavoured to increase the efficacy of the copper treatment by forcing it into the tissue by kataphoresis. For this purpose I have used a copper terminal which, with the intervention of a pad of cotton wool saturated with a 2-per-cent. copper sulphate solution, has been applied to the cocainised conjunctival surface of the everted lid. The strength of the current employed has been from 3 to 4 M.A., and the duration of the application varied from 2 to 5 minutes. The process is a decidedly painful one, and is followed by considerable hyperæmia. It is more painful than the application of the sulphate of copper stick, and I cannot say that so far I have found it any more efficacious. I have also, at the suggestion of Dr. Lewis Jones, tried treating the follicles in trachoma by puncturing them with a copper needle, and then passing through it a current of 2 to 3 M.A. for one minute. The hæmorrhage and hyperæmia occasioned prevent more than one or two follicles being dealt with satisfactorily at one sitting, but their absorption certainly seems to be promoted.

Wirtz,* in an article on "Ionic Therapeutics in Ophthalmology," says that in trachoma he has used a $\frac{1}{2}$ -per-cent. solution of copper sulphate with 2 to 3 M.A. for 2 to 3 minutes every few days, and that in four acute cases, after four weeks, the conjunctiva was nearly normal, and four

* Klinisch. Monatsblat. f. Augenheilk., November—December, 1908, and Ophthalmic Review, May, 1909, p. 149.

chronic cases were discharged cured "as far as one can speak of cure in trachoma."

In former times a more violent reaction than that excited by sulphate of copper was effected by the inoculation of gonorrhoeal matter. Mackenzie,* in writing of this practice, says: "Although it by no means appears a very safe one, it is undeniable that cures have been effected of the hypertrophied state of the conjunctiva, with the vasculo-nebulous condition of the cornea depending on it." The immense exudation of phagocytic polynuclear leucocytes which was in this way excited doubtless led to the invasion and disappearance of many of the follicles. It can be easily understood that in a tissue normally avascular like the cornea an increase in leucocytosis would be specially useful in promoting absorption of the lymphoid material.

On the introduction of jequirity the use of gonorrhoeal matter with its uncertain amount of reaction was abandoned. Now with Merck's extract of abrin, which has received the name "Jequiritol," we have a most efficacious means of exciting, by a chemical irritant, an acute inflammatory attack of limited duration. I have frequently employed it in cases with pannus with good effect. One application of Merck's strongest jequiritol usually suffices to produce the desirable amount of reaction. I have never found it to be so excessive as to necessitate the use of the anti-abrinic serum.

The X-ray treatment of trachoma has the advantage over all other methods of treatment in being painless. It was first introduced by Mayou in 1902, who, in writing of it, says†: "In the X-rays we have a method of setting up a leucocytosis with the absolute minimum of destruction of epithelial or other tissues; and, further, we have a means of producing an inflammation varying from a very slight leucocytosis to an actual gangrene of the part which, with due care and experience, we have under almost perfect control."

At the Ophthalmia Schools the X-ray treatment has

* Diseases of the Eye, 4th edit., p. 617.

† Changes produced by Inflammation in the Conjunctiva, p. 140.

been largely employed for trachoma with variable results. The method of application has been, first to keep the upper eyelid everted with a clamp holding the eyelashes and stuck with a strip of plaster to the forehead. This avoids exposure of the operator's fingers in any way to the rays. The patient is then seated a foot distant from the kathode of the Crooks tube and a five minutes' exposure is made with a current of 10 volts. These exposures are repeated each day for 10 days, and are then stopped for 10 days ; if at the end of that time little or no reaction has been set up, application for another 10 days is made.

Some cases treated in this way have steadily improved, follicles disappearing and pannus, when present, clearing up. Some, on the other hand, after very prolonged use of the rays, have shown but little amelioration. In no case have any disagreeable consequences been occasioned from the employment of X-rays in the cautious way above described. The varying results are, doubtless, to a great extent, attributable to varying degrees of dosage according to the hardness or softness of the tube employed. It would be very advantageous if some method for regulating the dosage in the X-ray treatment of trachoma could be introduced similar to the use of the Sabourand and Noiré pastilles in the treatment of ringworm by X-rays.

In 1904 I tried treating cases of trachoma with radium. A 5-milligramme glass tube of radium bromide of low radio-activity was held over the everted eyelids for five to seven minutes daily. This was continued for from 3 to 10 weeks before any definite reaction ensued. The results were not very encouraging. Probably with the improved apparatus for the application of radium introduced by Drs. Wickham and Degais, and longer exposures, more satisfactory effects might be obtained. Success in the treatment of trachoma by radium has been reported by Cohn,* Thieleman,† and Selenkowsky.‡

* Berliner Klin. Wochenschr., No. 1, 1905.

† Zeitschr. f. Augenh., December, 1905.

‡ Arch. f. Augenh., Bd. lx, 1908, H. 1, s. 63.

The third method by which a natural cure of trachoma is effected is, as already stated, the replacement of the adenoid layer by fibrous tissue. I would suggest that some of the more violent mechanical methods of treating trachoma which have been attended by good results act to a large extent by stimulating this natural tendency to fibrous tissue formation. The methods I refer to are those which may be included under the comprehensive term "grattage," whether carried out with a hard brush, a spiked iron instrument, or a knife blade.

I may conclude the description of my experience of the treatment of trachoma by saying that I have found it possible to so thoroughly eradicate the disease that it shows no tendency to relapse. In cases where a relapse seems to have taken place I believe the disease was never completely cured, or that some other inflammatory conjunctival infection (such as that due to Morax's diplobacillus) has become implanted in an eye showing the fibrous tissue sequelæ of trachoma.

I always mistrust statements as to the cure of trachoma in the course of a few weeks. Rapid and striking improvement in some cases is often made by treatment in the first weeks, but the complete cure of the disease, in my experience, always takes several months and sometimes years, whatever procedure be adopted.

I do not consider any case as satisfactorily cured so long as any follicular enlargements can be detected in any part of the conjunctiva, and until all abnormal discharge has ceased. To ensure that all follicular enlargements have been got rid of, a most careful scrutiny of the conjunctiva and all its folds has to be made. As an aid to such examination I have found the Binocular Magnifier, a modification of Berger's stereoscopic loupe, made for me by Messrs. E. W. Dixey and Son, of the greatest assistance.

To expose to view every part of the upper retrotarsal fold, after the eyelid has been everted in the usual way, a second eversion has to be made. This second eversion is

not usually referred to in text-books, but is of the greatest aid both in diagnosing, and estimating the progress of, a case of trachoma. I find it can be invariably performed with the fingers unaided by the use of any instrument. The upper eyelid having first been everted in the usual manner, a little pressure backwards is made on the free border of the tarsus with the forefinger; this raises its attached border away from the globe so that the thumb can be easily inserted beneath it. With the forefinger on the everted free border and the thumb beneath the attached border, the tarsus can be lifted away from the globe, exposing to view the retrotarsal fold. To expose the extreme angles of the upper retrotarsal fold, it is often necessary to transfer the tarsus, whilst held in this manner away from the globe, from the forefinger and thumb of one hand to the forefinger and thumb of the other. I sometimes nip up the retrotarsal fold whilst it is held exposed between my two thumbs to express follicles from it with my thumb nails.

It is probable that when the conjunctiva has its adenoid layer replaced by fibrous tissue its powers of resisting the attack of micro-organisms becomes lowered. I have frequently seen cases with fibrous tissue formation in the conjunctiva of long standing become the subjects of fresh attacks of inflammation. An examination of the discharge has revealed the presence of Morax's diplobacillus and the use of sulphate of zinc has soon cured the inflammation. Such cases were clearly not recurrences of trachoma.

I do not think that the reappearance of a vascular condition of the cornea as an accompaniment of fresh inflammation in an old case of trachoma necessarily implies a recurrence of that disease. We know that the tracks of the blood-vessels in the cornea when pannus subsides never completely disappear. Slight causes will sometimes lead to their fresh distention with blood. I have known it to occur as the result of an injury and I believe it may follow on any

undue hyperæmia of the conjunctiva, such, *e.g.*, that produced by some form of intercurrent conjunctivitis.

Whether or not the presence of "Prowazek granules" or "trachoma bodies" is to be regarded as a diagnostic sign of trachoma has yet to be decided. Clausen,* writing on this point, says: "The individual granules cannot be recognised with certainty, or considered as forming a standard for the diagnosis of trachoma, but when the specific granules are present, whether the small or large ones, absolutely specific clusters of them can be found near the nuclei of the epithelial cells, or else lying free."

Most observers have failed to find any histological difference between the follicles in the conjunctiva in trachoma and in other affections. Mayou has pointed out as characteristic of follicles affected with trachoma the absence of plasma cells in them, the scarcity of cells undergoing mitosis, and the presence of central necrotic changes. So far, the differentiation of trachoma from other affections, characterised by the presence of follicular enlargements, has rested on a clinical basis.

The close historical resemblance of the follicles, when ever enlarged, has led some observers to regard all conditions in which such enlargements are met with as stages of one and the same disease. Most, however, are now prepared to agree that there is one affection characterised by follicular enlargements, which are liable to be followed by fibrous tissue formation in the palpebral conjunctiva and involvement of the cornea with pannus, and other affections accompanied by follicular enlargements which never under any circumstances have such sequelæ. In countries where trachoma is rife, and where the majority of the inhabitants suffer from it, the recognition of different classes of cases with follicular enlargement is very difficult. In countries or localities where the disease which has the serious sequelæ, viz., trachoma, does not occur, the occurrence of affections accompanied by follicular enlargements without such sequelæ is readily realised.

* Trans. XI Congresso Internazion. di Oftalmol., 1909, p. 854.

The conditions in which non-trachomatous follicular enlargements occur may be classified as follows:—

(a) *In Atropine and Eserine Irritation.*—In atropine and eserine irritation, a very wide-spread enlargement of the follicles in the conjunctiva is sometimes met with. The clinical appearances presented by such a condition has, I think, features of its own which are distinctive. At any rate, I have found the form, the appearance, and distribution of the follicles such that I have been able to diagnose the condition, when I did not know previously that the drug which caused it had been used. The follicles are always small, very numerous, always discrete, scattered over the retrotarsal folds and tarsal conjunctiva. They are translucent and superficial in these two particulars, differing from early trachoma follicles on the tarsal conjunctiva, which appear set deep in the tissue and look like grey opaque areas.

(b) *In Children with a General Tendency to Adenoid Formations.*—Careful examination of the retrotarsal folds reveals small follicular swellings in a very large number of children who make no complaint of their eyes, who have no abnormal discharge from them, and no undue redness. Such children are frequently found to be also the subjects of new formation of adenoid tissue in the pharynx and nasopharynx. In some children these follicular enlargements in the conjunctiva may be very numerous, especially in the lower retrotarsal fold. They form rows of little rounded protuberances, never bigger than a pin's head, and have no tendency to run into one another and become confluent. When large, their presence may give rise to some irritation, causing the child to rub its eyes, or giving rise to blepharospasm. In such cases, hyperemia or inflammation may become superadded.

The diagnosis of this form of follicular enlargement from trachoma in its early stages rests on the position, size, and non-confluent character of the follicles. They are always located in the retrotarsal folds, never larger than a pin's

head, and do not run into one another. In the later stages of trachoma the tendency to fibrous tissue formation or involvement of the cornea are characteristic features.

(c) *In Mucopurulent Ophthalmia*.—As the result of the irritation of organisms which excite a mucopurulent ophthalmia, such as the Koch-Weeks bacillus, follicular enlargements may form in the retrotarsal folds. These remain discrete, and after a variable duration disappear, without either rupturing or causing any abnormal overgrowth of fibrous tissue.

To diagnose such cases from early cases of trachoma which commence as a mixed infection with acute symptoms, is often a matter of extreme difficulty. Indeed, in some it seems to me impossible to be quite sure of the diagnosis until the cases have been watched carefully for some weeks.

The presence of fibrous tissue formation in the conjunctiva, though such a frequent accompaniment of trachoma, is not pathognomonic of that affection. Besides occurring in the process of cicatrisation of injuries and burns, it may also be an accompaniment of other diseases.

In tubercle, in pemphigus, and in severe membranous ophthalmia portions of the conjunctiva become destroyed by ulceration. In the treating of these ulcers fibrous cicatricial tissue forms, producing an appearance closely resembling that seen in the late stages of a bad case of trachoma. So close may the resemblance be that the nature of the affection from which the condition arose can only be diagnosed by careful study of the history of the case.

Spring catarrh is another disease of the conjunctiva in which an extensive new fibrous tissue formation takes place. In this affection, unlike those first mentioned, the new formed fibrous tissue is not cicatricial fibrous tissue, it is not produced as a sequelæ of ulceration. It is one of the primary essential features of the disease. It grows forwards from the deeper layers, replaces the adenoid layer, and forms on the surface of the membrane the characteristic flat-topped elevations. In its non-cicatricial character it resembles

much of the fibrous tissue formation in trachoma, and the two diseases are also alike in the formation of large numbers of plasma cells which undergo degeneration, forming the hyaline material already referred to. Spring catarrh differs, however, from trachoma in the complete absence of follicular formation and also, as was first pointed out by Herbert, in the development of immense numbers of eosinophiles. A remarkable feature of the fibrous tissue formation in spring catarrh is the way in which it disappears as the disease subsides. It produces no contraction and leaves little if any sign of its former presence.

